PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43*bis*.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US2005/000482	07.01.2005	08.01.2004

International Patent Classification (IPC) or both national classification and IPC
A61K39/085, A61K39/09, A61P31/04

Applicant
IDAHO RESEARCH FOUNDATION, INC.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☒ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:

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WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US2005/000482

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☒ in written format

   ☒ in computer readable form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☒ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 1-17

because:

☒ the said international application, or the said claims Nos. 1-17 for industrial applicability relate to the following subject matter which does not require an international preliminary examination *(specify)*:

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the whole application or for said claims Nos. 1-4,9,11-13,15-17 (partially)

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	3,6,10
	No:	Claims	1-2,4-5,7-9,11-17
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-17
Industrial applicability (IA)	Yes:	Claims	-
	No:	Claims	-

2. Citations and explanations

see separate sheet

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

III. Non-establishment of opinion (Continuation)

1.1 Claims 1-17 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv)PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

1.2 Present claims 1-4,9,11-13,15-17 relate to a large number of possible methods. Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the methods claimed. In the present case, the claims lack support, and the application lacks disclosure. Consequently, the search and examination have been carried out for those parts of the claims which appear to be disclosed, namely those parts relating to the methods comprising administering disulfide loop region deletion mutants from staphylococcal enterotoxins or from Streptococcus pyrogenes toxins (see page 4, line 25 - page 5, line 6).

V. Reasoned statement (Continuation)

2 CITATIONS

Reference is made to the following documents:

D1: WO 01/60851 A (LG CHEMICAL LTD; LEE, HONG-KYUN; PARK, YONG-HO; HAN, KYU-BOEM; CHANG,) 23 August 2001 (2001-08-23)

D2: WO 99/27889 A (IDAHO RESEARCH FOUNDATION, INC; BOHACH, GREGORY, I) 10 June 1999 (1999-06-10)

3 NOVELTY (Art. 33(2) PCT)

3.1 D1 discloses a mutant Staphylococcal enterotoxin C molecule for use in a vaccine for preventing, alleviating and treating mastitis in cows. The mutant has a deletion in the

disulfide loop region and a substitution one amino acid, which inhibits formation of multiple structure (see page 3, line 10-17; page 4, line 5-15; page 5, line 23 - page 6, line 6; page 23, line 14 - page 27). In view of D1, the subject-matter of claims 1-2,4-5,7-9,11-17 is not considered to be novel.

3.2 The present application does not satisfy the criterion set forth in Article 33(2) PCT because the subject-matter of claims 1-2,4-5,7-9,11-17 is not new in respect of prior art as defined in the regulations (Rule 64(1)-(3) PCT).

4 INVENTIVE STEP (Art. 33(3) PCT)

4.1 Claim 1-3 are not considered to involve an inventive step because D1 discloses the use of a mutant Staphylococcal enterotoxin C molecule for the treatment of mastitis, a disease which is usually associated with elevated somatic cell levels in the milk (greater than 257000 per ml) and with reduced milk quality (see also description of the present application page 1, line 10-14). Consequently, treating the mastitis with the vaccine composition of D1 will result in a reduced number of somatic cells in milk and increased quality.

4.2 Claims 1-9,11-17 are not considered to be inventive, since there is no evidence in the application that these claims solve the problem of providing a method for reducing somatic cell count in milk and increasing the quality of milk over the broad scope of these claims. The description only provides support in the examples for the effect achieved by mutant SEC1-12.

4.3 For inventive step analysis of claim 10, D1 is considered to represent the most relevant state of the art and discloses a method for treating mastitis in cows comprising administering a mutant Staphylococcal enterotoxin C molecule. The mutant has a deletion of 12 amino acids in the disulfide loop region and a substitution. The subject-matter of claim 10 differs in that a method for treating mastitis comprising administering a mutant Staphylococcal enterotoxin C molecule having a deletion of 12 amino acids in the disulfide loop region is claimed

4.4 The problem to be solved by the subject matter of claim 10 may therefore be regarded as the provision of an alternative method for treating mastitis. The solution would be a method for treating mastitis comprising administering a mutant Staphylococcal enterotoxin C molecule having a deletion of 12 amino acids in the disulfide loop region.

4.5 This solution cannot however be considered as involving an inventive step (Article 33(3) PCT) because this specific mutant is disclosed in D2 (see page 8, line 18-24; table 4) and it would be obvious for the skilled person to use this mutant in a vaccine composition to treat mastitis and in this way lower the somatic cells in milk and increase the milk quality, especially since D1 started from the claimed SEC1-12 mutant to make the SEC-SER mutant, which differs by 1 amino acid from SEC1-12and has the properties of SEC1-12 and additionally has an improved stability.

4.6 The present application does therefore not satisfy the criterion set forth in Article 33(3) PCT and the subject-matter of claims 1-17 does not involve an inventive step (Rule 65(1)(2) PCT).

VII. Certain defects (Continuation)

5.1 Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in document D1 is not mentioned in the description, nor is this document identified therein.

VIII. Certain Observations (Continuation)

6.1 It appears from the description as a whole and in particular from the examples , that administering a **mutant staphylococcal enterotoxin C having a deletion in the disulfide loop region** is an essential technical feature of the methods of the present invention. This essential technical feature is however not present in independent claims 1 and 2. For this reason claims 1 and 2 lack clarity according to Art. 6 PCT taken in combination with Rule 6.3 (b) PCT (see also PCT Preliminary Examination

Guidelines III.4.3).

6.2 The relative term "modified" used in claim 12 has no well recognised meaning and leaves the reader in doubt as to the meaning of the technical features to which it refers, thereby rendering the definition of the subject-matter of said claim unclear (Art. 6 PCT).

6.3 The relative term "about" used in claims 15 and 16 has no well recognised meaning and leaves the reader in doubt as to the meaning of the technical features to which it refers, thereby rendering the definition of the subject-matter of said claims unclear (Art. 6 PCT).

6.4 The specification for an international application should be capable of being understood without reference to any other document (cf PCT Guidelines Ch. II 4.17). The expressions "hereby incorporated by reference" found in the description are therefore not according to the PCT requirements.

6.5 The vague and imprecise statement in the description on page 7, line 22-23 implies that the subject-matter for which protection is sought may be different to that defined by the claims, thereby resulting in lack of clarity (Article 6 PCT) when used to interpret them (see also the PCT Guidelines, PCT/GL/3 III, 4.3a).